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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,693	01/26/2001	Steven V. Beer	19603/2501 (CRF D-2375A)	6816

7590 05/27/2004

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/770,693	BEER ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of the Office action mailed 5 November 2003 is withdrawn in light of the new rejections below.

2. In light of Applicant statement that use of one DNA encoding a hypersensitive response elicitor would be obvious over use of another, the restriction among the groups is withdrawn and all claims are examined.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The Declaration of Steven Beer and David Bauer, filed 7 May 2004, overcomes the following rejections:

Claims 1-2, 6-7, 22-28, 30-31, 34-36, 39-41, 56-60, 62, 64-65, 68-70 and 72-73 under 35 U.S.C. 102(a) as being anticipated by Keller et al (1999, Plant Cell 11:223-235).

Claims 1-2, 5-10, 22-31, 34-36, 41-44, 56-60, 62-65, 70 and 73 under 35 U.S.C. 102(a) as being anticipated by Abdul-Kader et al (1999, Acta Hort. 489:247-250).

Claims 1-2, 5-10, 22-31, 34-38, 41-44, 56-67, 70-71 and 73 under 35 U.S.C. 103(a) as being unpatentable over Abdul-Kader et al in view of Scorza et al (1996, J. Amer. Hort. Sci. 121:616-619).

Claims 1-10, 22-36, 41-44, 56-65, 70-71 and 73 under 35 U.S.C. 103(a) as being unpatentable over Abdul-Kader et al (1999, Acta Hort. 489:247-250) in view of Pfitzner et al (1987, Nuc. Acids Res. 15:4449-4465).

Claims 1-4, 6-7, 22-28, 30-33, 34-36, 39-41, 56-62, 64-65 and 68-73 under 35 U.S.C. 103(a) as being unpatentable over Keller et al (1999, Plant Cell 11:223-235) in view of Pfitzner et al (1987, Nuc. Acids Res. 15:4449-4465).

Claims 1-2, 6-10, 22-28, 30-31, 34-44, 56-62 and 64-73 under 35 U.S.C. 103(a) as being unpatentable over Keller et al (1999, Plant Cell 11:223-235) in view of Zitter et al (US Patent 5,977,060, filed February 1997).

Claim Objections

5. Claims 35, 38, 40, 64, 67 and 69 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claimed plants would inherently be resistant to the listed oomycete species, and the claimed methods would inherently produce plants with resistance to those oomycete species; thus the claims fail to limit the parent claims.

6. Claims 14-15, 17-18, 20-21, 48-49, 51-52 and 54-55 are objected to because of the following informalities:

In claims 14, 17, 20, 48, 51 and 54, line 3, there is an improper article before "amino".

In claims 15, 18, 21, 49, 52 and 55, line 2, there is an improper article before "nucleotide".

Claim Rejections - 35 USC § 112

7. Claims 1-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chimeric genes encoding SEQ ID NOs:1, 3, 5 or 7 operably linked to the *gst1* promoter, with a secretion signal sequence, cells transformed with the construct, and oomycete-resistant plants transformed with the construct, does not reasonably provide enablement for constructs encoding any hypersensitive response elicitor from *E. chrysanthemi*, *E. amylovora*, *P. solanacearum* or *P. syringae*, from any other *Erwinia* or *Pseudomonas* species, or from any *Xanthomonas* or *Clavibacter* species at all operably linked to any promoter that is activated by an oomycete or cells and plants transformed with those constructs, or for constructs without a nucleic acid encoding a secretion signal peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 5 November 2003, as applied to claims 1-10, 22-44 and 56-73. Applicant's arguments filed 7 May 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to any chimeric gene comprising any oomycete activated promoter operably linked to a nucleic acid encoding any hypersensitive response elicitor with certain characteristics, with and without an operably linked nucleic acid encoding a secretion signal peptide, expression systems, cells, and plants comprising the chimeric gene, and a method of making a plant resistant to disease by transformation with the chimeric gene.

The instant specification, however, only provides guidance for the cloning of PCR amplification products of the *gst1* (*prp1*) promoter (SEQ ID NO:9) from potato, comparison of

the sequences of the clones to the published sequence, and construction of *gst1:uidA* constructs (example 1); *Agrobacterium*-mediated transformation of *Arabidopsis* with the constructs, inoculation of the transformed plants with *Peronospora parasitica* or *Pseudomonas syringae* pv *tomato* to show that the promoter induces expression in response to an oomycete and not to a bacteria (example 2), transformation of *Arabidopsis* with *gst1:hrpN* or *gst1*:secretion signal sequence:*hrpN* constructs and testing of the transgenic plants for resistance to *P. parasitica* - plants with the *gst1*:secretion signal sequence:*hrpN* construct were reported to be resistant, while the resistance status of plants transformed with the *gst1*: *hrpN* construct were not reported (example 3). The only hypersensitive response elicitors taught in the specification were SEQ ID NOs:2, 4, 6 and 8 from each of *E. chrysanthemi*, *E. amylovora*, *P. syringaes* and *P. solanacearum*, respectively.

The instant specification fails to provide guidance for nucleic acids encoding hypersensitive response elicitors within the full scope of the claims. The specification does not teach any nucleic acid encoding other hypersensitive response elicitors from *E. chrysanthemi*, *E. amylovora*, *P. solanacearum* or *P. syringae* or nucleic acids encoding hypersensitive response elicitors from any *Xanthomonas* or *Clavibacter* species or from any other *Erwinia* or *Pseudomonas* species.

The specification does not provide guidance for a representative number of nucleic acids encoding hypersensitive response elicitors from *E. chrysanthemi*, *E. amylovora*, *P. syringae* and *P. solanacearum*. For example, in *E. amylovora* there are at least 3 other nucleic acids encoding hypersensitive response elicitors: HrpW (Kim et al, 1998, J. Bacteriol. 180:5203-5210), dspE and dspF (Bogdanove et al, 2001, US Patent 6,228,644).

Expression of hypersensitive response elicitors that are not linked to secretion signal peptides do not produce pathogen resistant plants. Bauer et al (1999, Acta Hort. 489:301-304) transformed *Arabidopsis* plants with the *hrpN* gene expressed behind the *gst1* promoter and showed that the *hrpN* construct must be expressed with a signal sequence for export of the protein from the plants cells for production of resistant plants to be successful (pg 302, paragraph 5). Elicitors must be exported to the outside of the cell for functional interaction with membrane bound binding sites of the plant (Keller et al, 1999, Plant Cell 11:223-235, see pg 224, right column, paragraph 4; see also Bauer et al, pg 302, paragraph 6). The instant specification fails to teach the necessity for signal sequences for protein export.

The specification teaches no oomycete-inducible promoters other that *gst1*. Thus, the specification does not provide guidance for oomycete-inducible promoters within the full scope of the claims.

Given the claim breath and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant resummarizes the Wei Declaration of 1 August 2003 and urges that HrpN and HrpZ are conserved. Applicant urges that HR elicitors have a number of common characteristics and unique secondary structure, and cites He et al. Applicant urges that treatment of plants with HR elicitors resulted in disease resistance to a broad range of pathogens and enhanced plant growth and stress resistance (response pg 10-11).

This is not found persuasive because the rejection is not that nucleic acids encoding other hypersensitive response elicitors would not work in the method (as long as a nucleic acid encoding a secretion signal peptide was operably linked to that nucleic acid), but that nucleic

acids encoding hypersensitive response elicitors are not taught within the full scope of the claims.

Applicant urges that the specification teaches four hypersensitive response elicitor genes and that one of skill in the art could make others (response pg 11-12).

This is not found persuasive because the specification does not teach nucleic acids encoding hypersensitive response elicitors within the full scope of the claims. The specification does not teach how to make other such nucleic acids, as the specification is required to do for it to be enabling.

Applicant again urges that Belbahri et al confirmed the breath of the instant application by showing that plants transformed with constructs comprising the hsr203J promoter and a nucleic acid encoding PopA had oomycete resistance. Applicant urges that they and Belbahri have demonstrated that the application is enabled, and that any hypersensitive response elicitor (HRE) protein can be used in the instant invention (response pg 12).

This is not found persuasive because the rejection is not that nucleic acids encoding hypersensitive response elicitors would not induce pathogen resistance when transformed into a plant, but that nucleic acids encoding hypersensitive response elicitors and comprising oomycete-induced promoters are not taught within the full scope of the claims.

Applicant urges that the instant application teaches three other hypersensitive response elicitor genes and that any hypersensitive response elicitor gene can be used (response pg 13).

This is not found persuasive. There are at least 12 *Erwinia* species, 113 *Pseudomonas* species, 2 *Clavibacter* species and 68 *Xanthomonas* species. The specification only teaches a single nucleic acid encoding a hypersensitive response elicitor from each of two *Erwinia* and two

Pseudomonas species. The specification teaches no nucleic acids encoding a hypersensitive response elicitor from a *Xanthomonas* or *Clavibacter* species. Thus, nucleic acids encoding hypersensitive response elicitors are not taught within the full scope of the claims.

Applicant urges that the specification enables one to practice the invention with any oomycete-inducible promoter, including *gst1*, and one of skill in the art could identify if a promoter is oomycete inducible, using processes known in the art, citing Keller, and use such promoters in the instant methods, constructs and plants (response pg 13-14).

This is not found persuasive. Although there are a number of oomycete induced promoters taught in the art, the specification itself only teaches one.

See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

8. Claims 1-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 5 November 2003, as applied to claims 1-10, 22-44 and 56-73. Applicant's arguments filed 7 May 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of any chimeric gene comprising any oomycete activated promoter operably linked to a nucleic acid encoding any hypersensitive response elicitor with certain characteristics, with and without an operably linked nucleic acid encoding a secretion signal peptide, expression systems, cells, and plants comprising the

chimeric gene, and a method of making a plant resistant to disease by transformation with the chimeric gene. In contrast, the only nucleic acids encoding hypersensitive response elicitors described specification are SEQ ID NOs:2, 4, 6 and 8, and the only oomycete-specific promoter described in the specification is SEQ ID NO:9. Applicant does not describe other nucleic acids encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described chimeric genes comprising any oomycete activated promoter operably linked to a nucleic acid encoding any hypersensitive response elicitor with certain characteristics within the full scope of the claims. Because the chimeric genes are not described within the full scope of the claims, the methods of using the chimeric genes to produce path-gene resistant plants are likewise not described. Thus, the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

Applicant urges that the Office must consider all species disclosed in the application not just *E. amylovora*, and four HRE genes are disclosed (response pg 14-15).

This is not found persuasive. The four HRE genes described in the specification have been considered, but they do not describe the full scope of the HRE genes used in the claimed constructs, plants and methods.

Applicant urges that as demonstrated in the Wei Declaration, $harpin_{Ea}$ is a representative species belonging to an art-recognized class of hypersensitive response elicitors and that results

achieved with one member have proven to be similarly achieved with other members of the class (response pg 15).

This is not found persuasive because the specification does not describe nucleic acids within the full scope of the claims.

Applicant urges that the specification describes a representative number of proteins that contain substantially no cysteine, are glycine rich, heat stable, hydrophilic, and elicit HR (response pg 15).

This is not found persuasive. In *E. amylovora* there are at least three other hypersensitive response elicitor protein genes: the HrpW gene (Kim et al, 1998, J. Bacteriol. 180:5203-5210) and the dspE or dspF genes (Bogdanove et al, 2001, US Patent 6:228,644). Thus, the instant specification fails to describe a representative number of nucleic acids that encode hypersensitive response elicitor proteins from *E. amylovora*, much less any *Erwinia, Pseudomonas, Clavibacter* or *Xanthomonas* species.

Applicant urges that the Office cites no relevant evidence that the four species are not representative of the genus (response pg 15-16).

This is not found persuasive. The instant claims are drawn to use of a nucleic acid encoding a hypersensitive response elicitor from any *Erwinia, Pseudomonas, Clavibacter* or *Xanthomonas* species. The specification, however, describes only four such nucleic acids.

There are at least 12 *Erwinia* species, including *E. amylovora, E. aphidicola, E. billingiae, E. carotovora, E. chrysantum, E. mallotivora, E. papayae, E. persicina, E. psidii, E. pyrifoliae, E. rhapontici,* and *E. tracheiphila.* The instant specification only describes two nucleic acids encoding hypersensitive response elicitors from two species.

There are at least 113 *Pseudomonas* species, including *P. abietaniphila, P. agarici, P. agarolyticus, P. alcaligenes, P. alcaliphila, P. alginovora, P. amygdali, P. anguilliseptica, P. andersonii, P. asplenii, P. aurantiaca, P. avellanae, P. azelaica, P. azotoformans, P. balearica, P. batumici, P. borealis, P. brassicacearum, P. brenneri, P. cannabina, P. caricapapayae, P. cichorii, P. coronafaciens, P. cedrina, P. congelans, P. corrugata, P. chloritidismutans, P. chlororaphis, P. citronellolis, P. costantinii, P. cremoricolorata, P. denitrificans, P. diterpeniphila, P. extremorientalis, P. flavescens, P. ficuserectae, P. filiscindens, P. fluorescens, P. fragi, P. frederiksbergensis, P. fulgida, P. fulva, P. fuscovaginae, P. gessardii, P. gingeri, P. graminis, P. grimontii, P. halodenitrificans, P. halophila, P. hibiscicola, P. hydrogenovora, P. indica, P. japonica, P. jessenii, P. jinjuensis, P. kilonensis, P. koreensis, P. libanensis, P. lini, P. lundensis, P. lurida, P. lutea, P. luteola, P. mandelii, P. marginalis, P. mediterranea, P. meliae, P. migulae, P. mucidolens, P. marginata, P. meridiana, P. mendocina, P. monteilii, P. mosselii, P. nitroreducens, P. oleovorans, P. orientalis, P. oryzihabitans, P. pseudoalcaligenes, P. palleroniana, P. parafulva, P. pavonanceae, P. pertucinogena, P. proteolytica, P. psychrophila, P. resinovorans, P. poae, P. plecoglossicida, P. putida, P. rathonis, P. reactans, P. rhizosphaerae, P. rhodesiae, P. salomonii, P. stutzeri, P. syringae, P. savastanoi, P. straminea, P. synxantha, P. tolaasii, P. trivialis, P. tremae, P. taetrolens, P. thermaerum, P. thermocarboxydovorans, P. thermotolerans, P. thivervalensis, P. umsongensis, P. vancouverensis, P. veronii, P. viridiflava, P. wisconsinensis,* and *P. xiamenensis.* The instant specification only describes two nucleic acids encoding hypersensitive response elicitors from two species.

There are at least 68 *Xanthomonas* species, including *X. albilineans, X. arboricola, X. axonopodis, X. bromi, X. campestris, X. cassavae, X. citri, X. codiaei, X. cucurbitae, X. cynarae,*

X. fragariae, X. gardneri, X. hortorum, X. hyacinthi, X. melonis, X. oryzae, X. pisi, X. populi, X. sacchari, X. theicola, X. translucens, X. vasicola, and *X. vesicatoria.* The instant specification does not describe any nucleic acids encoding hypersensitive response elicitors from any *Xanthomonas* species.

There are at least 2 *Clavibacter* species, including *C. michiganensis* and *C. xyli*. The instant specification does not describe any nucleic acids encoding hypersensitive response elicitors from any *Clavibacter* species.

As the many, if not the majority, of the species listed above would produce at least one hypersensitive response elicitor, it is clear that the genus of nucleic acids encoding hypersensitive response elicitors within the recited genera is not fully described, and the entire genus of nucleic acids encoding hypersensitive response elicitors from any bacteria or fungus is not described. Thus, the instant specification fails to describe nucleic acids encoding hypersensitive response elicitors within the full scope of the claims, and thus fails to describe methods of using those nucleic acids.

Not only is written description lacking for nucleic acids encoding hypersensitive response elicitors within the full scope of the species within the claims, as discussed above, the existence of DspE, DspF and HrpW demonstrates that even within a single species, description of only one such nucleic acid fails to describe nucleic acids encoding hypersensitive response elicitors within the full scope of the claims.

Lastly, the specification does not describe more than one *gst1* promoter.

9. Claims 1-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 5 November 2003, as applied to claims 1-10, 22-44 and 56-73. Applicant's arguments filed 7 May 2004 have been fully considered but they are not persuasive.

The term "glycine rich" in claim 1 is a relative term that renders the claim indefinite. The term "glycine rich" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. How many or what proportion of glycine distinguishes a glycine rich protein from one that is not?

Applicant urges that they demonstrated in the Wei Declaration that bacterial hypersensitive response elicitors are an art-recognized class, and cite Buttner et al and Alfano et al; thus one of skill in the art would understand the term even though it does not have an exact numerical meaning (response pg 17).

This is not found persuasive. The metes and bounds of the claims are unclear because the cutoff for a protein being "glycine-rich" or not being "glycine-rich" is unclear.

The following rejections are new:

Claims 1 and 73, line 3, and claims 7-8, 11-13, 16, 19, 27, 41-42, 45-47, 50, 53 and 70, line 2 are indefinite in their recitation of "protein or polypeptide derived from a bacterial plant pathogen". It is unclear how the protein or polypeptide differs from the native protein or polypeptide in the pathogen.

The term "substantially no cysteine" in claim 1 is a relative term that renders the claim indefinite. The term "substantially no cysteine" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. How many or what proportion of cysteine distinguishes a protein with substantially no cysteine from one that has a substantially number of cysteines?

Claim Rejections - 35 USC § 103

10. Claims 1, 7-27, 30, 35-61 and 64-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer et al (1998, US 5,850,015) in view of each of Doerner et al (1990, Bio/Technol. 8:845-848) and Kawamata et al (1997, Plant Cell Physiol. 38:792-803).

The claims are drawn to a chimeric gene comprising an oomycete activated promoter operably linked to a nucleic acid encoding a hypersensitive response elicitor, expression systems, cells, and plants, including tobacco and grape, comprising the chimeric gene, and a method of making a plant, including tobacco and grape, resistant to disease by transformation with the chimeric gene.

Bauer et al disclose constructs comprising a pathogen-inducible promoter operably linked to a nucleic acid encoding a hypersensitive response elicitor from *E. chrysanthemi*, host cells and plants, including tobacco and grape, transformed with them, and a method of using the constructs to impart pathogen resistance to plants, including tobacco and grape, wherein the constructs are transformed into plants by Agrobacterium mediated transformation or particle bombardment (claims 1-19). Bauer et al suggest using the pathogen-inducible promoters from phenylalanine

ammonia lyase (PAL) and chalone synthase (CHS) genes (column 13, lines 25-39), but do not disclose the sequence of such promoters.

Doerner et al teach the bean CHS promoter, which is induced by an oomycete (pg 848, leftt column, paragraph 5; pg 847, left column, paragraph 1).

Kawamata et al teach a pea PAL promoter, which is induced by oomycetes (Figure 1; paragraph spanning the columns on pg 798).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of imparting pathogen resistance to plants as taught by Bauer et al, to use the pathogen-inducible promoters from PAL and CHS genes as described in each of Doerner et al and Kawamata et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Bauer et al to do so (column 13, lines 25-39). One of skill in the art would know that the expression constructs would also require a 3' regulatory region to get proper expression the nucleic acid encoding the hypersensitive response elicitor. Substitution of one nucleic acid encoding a hypersensitive response elicitor for another would be obvious over the use of any other nucleic acid encoding a hypersensitive response elicitor, as per Applicant admission in the response filed 7 May 2004.

11. Claims 2-4, 28, 31-33 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer et al in view of each of Doerner et al and Kawamata et al as applied to claims 1, 7-27, 30, 35-61 and 64-72 above, and further in view of Gopalan et al (1996, Plant Cell, 8:1095-1105).

The claims are drawn to a chimeric gene comprising an oomycete activated promoter operably linked to a nucleic acid encoding a signal peptide operably linked to a nucleic acid encoding a hypersensitive response elicitor, expression systems, cells, and plants, including

tobacco and grape, comprising the chimeric gene, and a method of making a plant, including tobacco and grape, resistant to disease by transformation with the chimeric gene.

The teachings of Bauer et al in view of each of Doerner et al and Kawamata et al are discussed above. Bauer et al in view of each of Doerner et al and Kawamata et al do not disclose the use of nucleic acids encoding signal peptides in the constructs.

Gopalan et al teach the use of a nucleic acid, SEQ ID NO:12, encoding a signal peptide of SEQ ID NO:13 in constructs for expressing the hypersensitive response eliciting protein avrB (pg 1098, right column, paragraph 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of making a plant resistant to disease by transformation with the chimeric gene as taught by Bauer et al in view of each of Doerner et al and Kawamata et al, to use a nucleic acid encoding a signal peptide in the construct as described in Gopalan et al. One of ordinary skill in the art would have been motivated to do so because Gopalan et al teaches that the signal peptide sequence was required to obtain viable transformants and that death of transformants without the signal peptide was the result of high levels of the hypersensitive response eliciting protein inside cells (pg 1098, right column, paragraph 1).

12. Claims 1-2, 7-28, 30-31, 35-44, 56-62 and 64-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chappell et al (US Patent 5,981,843, filed May, 1995) in view of Zitter et al (US Patent 5,977,060, filed February 1997). The rejection is modified from the rejection set forth in the Office action mailed 5 November 2003, as applied to claims 1-2, 6-10, 22-28, 30-31, 34-44, 56-62 and 64-72. Applicant's arguments filed 7 May 2004 have been fully considered but they are not persuasive.

The claims are drawn to a chimeric gene comprising an oomycete activated promoter operably linked to a nucleic acid encoding a signal peptide, which is operably linked to a nucleic acid encoding a hypersensitive response elicitor, expression systems, cells, and grape plants comprising the chimeric gene, and a method of making a grape or tobacco plant resistant to disease by transformation with the chimeric gene.

Chappell et al teach chimeric genes comprising a DNA molecule encoding a hypersensitive response elicitor from *Phytophthora* (the *parA1* elicitin) and operably linked to that, an oomycete-activated promoter (the EAS4 promoter) (column 20, lines 1-52). GenBank Accession No. U12639 teaches that the pBI101 vector in which this construct was made has the 3'UTR of the nopaline synthase gene as a 3' regulatory region. Chappell et al also teach tobacco plants transformed with the construct, plant and *Agrobacterium* cells comprising the construct, and a method of using it to produce a plant with pathogen resistance (Fig. 3, and claims 14-38). These plants would be resistant to oomycetes like *Phytophthora* and *Peronospora* (column 2, lines 55-67). ParA1 elicitin inherently comprises a signal peptide (column 3, lines 34-35, and column 20, lines 12-13). The EAS4 promoter would comprise an "effective fragment" of the *gst1* promoter. Chappell et al also teach ballistic transformation of the plant cells (column 17, lines 1-9). The plants of Chappell et al are indistinguishable from plants derived from rootstock. Chappell et al do not disclose the use of a nucleic acid encoding hrpN in the constructs.

Zitter et al teach a nucleic acid encoding hrpN and plants and seeds, including grape, transformed with hypersensitive response elicitors from *E. amylovora* (claims 32-44; SEQ ID NO:3).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the constructs used in the method of producing pathogen-resistant plants taught by Keller et al, to use the nucleic acid encoding hrpN described in Zitter et al. One of ordinary skill in the art would have been motivated to do so because substitution of one nucleic acid encoding a hypersensitive response elicitor for another is an obvious design choice. The method of transformation would be an obvious design choice. Substitution of one nucleic acid encoding a hypersensitive response elicitor for another would be obvious over the use of any other nucleic acid encoding a hypersensitive response elicitor, as per Applicant admission in the response filed 7 May 2004.

Applicant urges, citing Ponchet et al, that fungal elicitins are not known to resemble any other class of proteins and are classified by source, size, presence of cysteine residues and synthesis as preproteins. Applicant also urges that avirulence proteins are effectors proteins, citing Buttner et al and Collmer et al, that trigger an R-gene specific plant defense resulting in a hypersensitive response. Applicant also urges that harpin proteins are glycine rich, substantially free of cysteine, heat stable, hydrophilic and elicit a hypersensitive response, citing He et al, Buttner et al, and Collmer et al. (response pg 19-20).

This is not found persuasive because all the proteins induce a hypersensitive response.

Applicant urges that because Chappell et al defines elicitin in a manner contrary to the commonly accepted definition of the term, that is to include avirulence proteins, one of ordinary skill in the art would not know which proteins are considered by Chappell as having similar effects on the hypersensitivity response as ParA1 elicitin; thus, one of ordinary skill in the art would not believe Chappell to suggest use of harpins (response pg 20).

This is not found persuasive because Chappell's definition, which emphasizes the hypersensitive response eliciting function of the protein would suggest to one of skill in the art that other hypersensitive response eliciting proteins, including harpins, could be used in the method and constructs.

Furthermore, it is noted that Applicant calls elicitins hypersensitive response elicitors. See the instant specification on pg 8, lines 28-32, which states "Exemplary hypersensitive response elicitor proteins or polypeptides from fungal sources include, without limitation, the hypersensitive response elicitors (i.e., elicitins) from various *Phytophthora* species (e.g., *Phytophthora parasitica, Phytophthora cryptogea, Phytophthora cinnamomi, Phytophthora capsici, Phytophthora megasperma, Phytophthora citrophthora*, etc.)." See also the paragraph spanning pg 18-19. Thus, one of skill in the art would consider use bacterial hypersensitive response elicitors in the invention of Chappell.

Applicant urges that Chappell's teachings of the use of harpins only for inducing expression of the encoded elicitins would suggest to one of ordinary skill in the art that harpins should not be used in the chimeric gene (response pg 20).

This is not found persuasive because Chappell defines elicitins as proteins produced by plant pathogens that induce HR (column 1, line 66, to column 2, line 1).

13. Claims 5-6, 29, 63 and 73 are free of the prior art, given the failure of the prior art to teach or suggest chimeric genes comprising the gst1 promoter operably linked to a nucleic acid encoding a hypersensitive response elicitor, cells, and plants comprising the chimeric gene, and a method of making a plant resistant to disease by transformation with the chimeric gene.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (571) 272-0547.

Anne R. Kubelik, Ph.D.
May 25, 2004